II. REMARKS

Claims 2 to 14 are pending.

A. Regarding the Amendments

The specification has been amended to recite Sequence Identifiers. It is noted that underlining of the volume numbers of the references cited at page 26 of the application was present in the application as filed, and does not indicate material being added. As such, the amendments merely address a formality, and do not add new matter.

Claim 2 has been amended to clarify that the "cell proliferative disorder" is a "growth differentiation factor-5 (GDF-5) associated" cell proliferative disorder, and to clarify that a GDF-5 specific antibody "specifically binds a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO:10 or SEQ ID NO:13". The amendments are supported, for example, at page 15, lines 6-17, and by Figures 2 and 3A, which disclose SEQ ID NO:10 and SEQ ID NO:13, respectively. In addition, claim 2 has been amended to clarify that "an increased or decreased level of binding to the specimen as compared to binding to a normal cell is indicative of a GDF-5 associated cell proliferative disorder". The amendment is supported, for example, at page 15, lines 14-16. As such, it is submitted that the amendments to claim 2 do not add new matter.

Claim 14 has been amended to depend from claim 13, which provides the requisite antecedent basis. The amendment merely addresses an informality and, therefore, does not add new matter.

B. Regarding the Species Election

It is maintained in the Office Action that the requirement to elect a species was proper and, therefore, that Applicants' election of the species of "a detectable label" and "a fluorescent compound" has been made final. Applicants acknowledge the finality of the species election for

purposes of examination. It is noted, however, that the references cited in the present Office Action do not appear to be based on or encompass "a fluorescent compound". As such, it is respectfully requested that, upon finding the examined subject matter allowable, the Examiner consider the allowability of a generic claim to "a detectable label" and further examine the additional species set forth in the claims, as indicated in the Communication mailed October 2, 2002 (Paper No. 8, page 3; see, also, 37 CFR 1.146).

C. Regarding Compliance with the Sequence Rules

It is noted in the Office Action that the specification was not fully in compliance with the requirements under 37 C.F.R. §§ 1.821-1.825. The specification has been amended to attend to this informality. As such, it is respectfully requested that this objection to the specification be withdrawn.

D. Rejections under 35 U.S.C. § 112

The objection to the specification and corresponding rejection of claims 2 to 8, 11 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, are respectfully traversed.

It is acknowledged in the Office Action that the specification is enabling for a method of detecting GDF-5 comprising the amino acid sequence shown in Figure 2. In this respect, Applicants point out that the claims have been amended to clarify that antibody useful in the claimed methods "specifically bind a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO:10 or SEQ ID NO:13", and that the recited sequences include that shown in Figure 2, as well as the mature C-terminal GDF-5 polypeptide shown in Figure 3A.

It is alleged in the Office Action, however, that the specification does not enable detecting any and/or all cell proliferative disorders or a uterine neoplasm, endometrioses or a skeletal disorder by detecting GDF-5 because the claims do not require, for example, detecting an increase or decrease in GDF-5 expression is associated with the disorder. In this respect, Applicants point out that the claims have been further amended to clarify that the claimed

methods are directed to detecting a cell proliferative disorder "associated with GDF-5" by detecting an increased or decreased level of GDF-5 expression in a cell of a specimen as compared to a corresponding normal cell.

It is further alleged in the Office Action that the specification does not disclose whether an increase or decrease in GDF-5 expression is associated with a cell proliferative disorder. Applicants submit, however, that the specification discloses that GDF-5 is expressed primarily in uterine tissue in adults (Example 2) and in uterine tissue and the skeletal system in embryos (Example 3). Further, it is known in the art that other GDF polypeptides such as GDF-8 (myostatin) have an effect on the tissue in which they are expressed (e.g., muscle). As such, the skilled artisan reasonably would have known that GDF-5, which is expressed primarily in uterine tissue in adults, and in uterine tissue and the skeletal system in embryos, effects the growth and differentiation of these tissues and, therefore, can be associated with a cell proliferative disorder of these tissues, as well as of tissues in which the GDF-5 is expressed at lower levels.

In view of the amendments, and for the reasons set forth above, it is submitted that one skilled in the art, viewing the specification, would have known how to practice the claimed methods without undue experimentation. Accordingly, it is respectfully requested that this objection to the specification be withdrawn, and that the corresponding rejection of claims 2 to 8, 11 and 12 as allegedly lacking enablement be removed.

The objection to the specification and corresponding rejection of claims 2 to 8, 11 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, are respectfully traversed.

It is stated in the Office Action that the specification uses the term "GDF-5" broadly, to encompass polypeptides having substitutions and other modifications as compared to the GDF-5 polypeptide disclosed in Figures 2 and 3. As such, it is alleged that undue experimentation would have been required for the skilled artisan to obtain an antibody useful in the methods as broadly considered. Applicants point out, however, that the amended claims require use of an antibody that "specifically binds a GDF-5 polypeptide having an amino acid sequence as set

forth in SEQ ID NO:10 or SEQ ID NO:13". As such, the skilled artisan would have known that a polypeptide comprising SEQ ID NO:10 or SEQ ID NO:13 would be used to prepare an antibody useful in the claimed methods, and would have known how to make such an antibody using well known and routine methods. Accordingly, it is respectfully requested that this objection to the specification be withdrawn, and that the corresponding rejection of claims 2 to 8, 11 and 12 as allegedly lacking enablement be removed.

The objection to the specification and corresponding rejection of claims 2 to 8, 11 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking an adequate written description, are respectfully traversed.

The rejection is based on the broad definition in the specification of "GDF-5" as set forth in the enablement rejection (above). For the reasons set forth above, it is submitted that the subject application clearly describes an antibody that specifically binds a GDF-5 having a sequence as set forth in SEQ ID NO:10 or SEQ ID NO:13 such that the skilled artisan would have known that Applicants were in possession of such antibodies and, therefore, of the claimed method. Accordingly, it is respectfully requested that the objection to the specification be withdrawn, and that the corresponding rejection of claims 2 to 8, 11 and 12 as allegedly lacking an adequate written description be removed.

The rejections of claims 2 to 8, and 11 to 14 under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite is respectfully traversed.

It is alleged in the Office Action that claims 2 to 8, 11 and 12 are indefinite in reciting the term "GDF-5", as it is unclear as to the material limitations placed on the claim by this element. Claim 2 has been amended to more clearly indicate that the term "GDF-5" refers to "growth differentiation factor-5", and that an antibody useful in a method of the invention is one that "specifically binds to a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO:10 or SEQ ID NO:13". As such, it is submitted that the subject matter of claims 2 to 8,

11 and 12 are clearly defined and, therefore, respectfully requested that this ground of rejection be removed.

It is also alleged that claim 14 is indefinite in reciting the term "the solid phase carrier" because the term lacks antecedent basis, and because the term "modified cellulose" is not defined such that the limitations of the element cannot be determined. Claim 14 has been amended to depend from claim 13, which provides the requisite antecedent basis for "the solid phase carrier". As such, it is respectfully requested that this ground of rejection be removed.

With respect to the term "modified cellulose", it is submitted that one skilled in the art, reading the claim in view of the claimed subject matter (i.e., an immunologic method for detecting a protein) and of the specification (e.g., page 15, line 18, to page 16, line 10, describing such immunoassays), would have known the metes and bounds of modified cellulose useful for the claimed methods. Further, it is submitted that the skilled artisan would know many examples of modified cellulose products useful in such a method, including, for example, nitrocellulose (see Exhibit A), BrCN-modified cellulose (see Exhibit B; see, also, Exhibit C), carboxymethyl-cellulose (CM-cellulose; see Exhibit C), diethylaminoethyl-cellulose (DEAE-cellulose), and the like. As such, it is respectfully requested that this ground of rejection be removed.

In view of the amendments, and for the reasons set forth above, it is submitted that one skilled in the art, reading the claims, would know the metes and bounds of the claimed subject matter. Accordingly, it is respectfully requested that the rejections of claims 2 to 8, and 11 to 14 under 35 U.S.C. § 112, second paragraph, be removed.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect respectfully is requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Dated: May 27, 2003

Richard J. Imbra
Registration No. 37,643
Telephone: 858-677-1496
Facsimile: 858-677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133

Customer Number 28213